Title	Study of Ring-Opening Reaction of Spiro[5.2]octenes with Aqueous Hydro-halic Acid: Substituent Effect on the Regioselectivity
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Stereocontrolled Synthesis of Spiro[n.2]alkenes by Ring Contraction of Fused-Cyclobutanols

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Abstract: Unusual ring contraction rearrangement giving spiro-cyclopropanes from fused-cyclobutanols have been developed. It is found that the strain energy of substrates derived from an additional fused-ring and the stereoelectronic effect of the migrating σ-bond are important factors. It is noteworthy that the rearrangement proceeds in a stereospecific manner. Moreover, the method provides spiro(cyclopropane-indane) framework from tricyclo[6.3.0.0^{2,5}]undecane, which corresponds to illudane and the protoilludane skeleton, respectively.

Keywords: small rings · ring contraction · rearrangements · spiro compounds · stereocontrolled synthesis

Introduction

Small ring systems are an important topic in organic chemistry, and afford considerable attention from theoretical, synthetic and medicinal perspectives. Spirocyclic compounds have also attracted to synthetic and medicinal chemists because of their characteristic structure. Spiro[n.2]alkanes and alkenes are found in naturally occurring substances,[1] such as illudins (Figure 1). Illudin S (**1**) was first discovered as an antibiotic from the Jack O'Lantern mushroom *Omphalotus olearius*. Irofulven (**2**), which is a hemi-synthetic analog derived from illudin S, has been developed as an anticancer drug candidate, and is currently in clinical trials for use in solid tumor treatments (Phase II).[2] On the basis of the structures of its metabolites and structure-activity relationship studies, it has been proposed that the spiro-cyclopropyl structure plays a key function in anticancer action.[3] Illudins were postulated to be bio-synthesized through 6-protoilludene (**3**) by a ring contraction rearrangement.[4],[5] This biosynthetic mechanism led us to believe that the spiro[n.2]alkenes skeleton would be chemically transformed from fused-cyclobutanols.

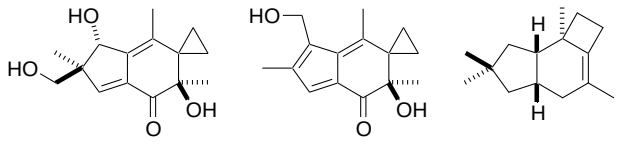

Figure 1. Illudin S and its related compounds

Due to the inherent ring strains of small ring systems, interesting aspects of their reactivity have been well exploited.[6],[7] For example, ring expansion rearrangement reactions have been well studied. Furthermore, relief of the ring strain is known to produce cyclobutane and cyclopentane compounds from cyclopropane and cyclobutane derivatives, respectively, by the migration of a C-C bond in the ring system.[8] Conversely, the reversal rearrangement reaction (ring contraction), which produces a smaller ring system, is also possible.[6c],[9] Olah *et al* have summarized the nature of cyclopropylcarbinyl cations, which can be rearranged into cyclobutyl cations, and their reactivity.[10] However, studies concerning the selective formation of cyclopropyl compounds from cyclobutanes are rare for thermodynamic reasons.[11] We believe that an increase in strain energy of a cyclobutane substrate through the installation of an additional ring would induce the ring contraction rearrangement in a cyclopropane compound (Figure 2). Thus, planar conformation of sp^2 carbocation on the bridgehead of fused-cyclobutane **C** would be thermodynamically unfavourable owing to the conformational restriction. PM3 level calculations estimate the heat of formation (ΔH_f) of the monocyclic cyclobutyl cation **A** and the corresponding cyclopropylcarbinyl cation **B** to be 190.17 and 192.60 kcal/mol, respectively. On the other hand, the ΔH_f for cations possessing bicyclo[4.2.0]octane **C** and spiro[4.2]octane **D** were calculated to be 191.87 and 190.18 kcal/mol, respectively. In this paper, we describe the unusual ring contraction reaction of fused-cyclobutanols producing spirocyclic cyclopropanes, spiro[n.2]alkenes, as well as provide mechanistic insight. To the best of our knowledge, stereocontrolled methods giving spiro[n.2]alkenes bearing substituents on cyclopropane ring,

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which would be a useful skeleton in medicinal and synthetic chemistry, are quite limited.[12]

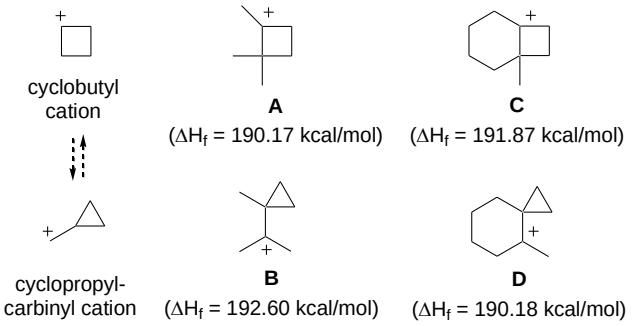
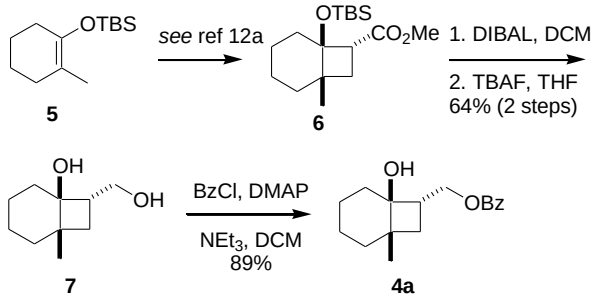


Figure 2. PM3 calculated heat of formation of tertiary cyclobutyl cations **A**,**C** and cylopropylcarbinyl cations **B**,**D**.

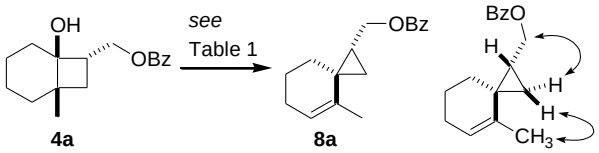
Results and Discussion

Cyclobutanol substrates **4a-j** were prepared from silyl enol ethers in several steps. A typical synthetic route of **4a**, which corresponds to a precursor of **C** (Figure 2), is summarized in Scheme 1. Siloxycyclobutane **6** was synthesized from silyl enol ether **5** and methyl acrylate by a Tf_2NH-catalyzed [2 + 2] cycloaddition, which was previously developed by us giving substituted cyclobutanes in a concise manner.[13] Reduction of ester moiety of **6**, followed by desilylation, gave diol **7**. Selective protection of the primary hydroxyl group of **7** afforded **4** in a good yield.



Scheme 1. Typical procedure for the preparation of substrate **4a**. TBS = *tert*-butyldimethylsilyl, DIBAL = diisobutylaluminum hydride, DCM = dichloromethane, TBAF = tetra-*n*-butylammonium fluoride, THF = tetrahydrofuran, Bz = benzoyl, DMAP = 4-dimethylaminopyridine

With a series of cyclobutanols in hand, we examined the ring contraction reaction of **4a** under conditions for the formation of the cyclobutyl cation (Scheme 2). When **4a** was treated with several acid catalysts, such as conc. H_2SO_4, $TsOH \cdot H_2O$ and $BF_3 \cdot OEt_2$, a complex mixture was obtained but no cyclopropane compound was detected. Next, we presumed hat the transformation of the hydroxyl group of **4a** into a good leaving group would induce the desired rearrangement (Table 1). Under the conditions of Sc(III)-catalyzed acetylation,[14] the desired cyclopropane **8a** was formed in 41% yield but the major product was the corresponding acetate (entry 1). Treatment of **4a** with methanesulfonyl chloride (MsCl; 4.5 equiv.) in the presence of excess amounts of 2,6-lutidine gave positive results (entries 2-4). These results indicate that polar solvents are preferable for the reaction. Using 2,6-lutidine as a solvent, the ring contraction proceeded smoothly, producing **8a** in 70% yield (entry 5). When the reaction was performed using smaller amounts of the reagent or at a lower temperature, the chemical yield of **8a** was reasonable but the reaction required a longer time to complete (entries 6 and 7). In all cases, spiro[4.2]octene **8a** was obtained as a single diastereomer, whose structure as well as stereochemistry were determined by 2D-NMR experiments. It should be noted that no compound that could be formed by the rearrangement of another σ-bondwere was detected. When thionylchloride ($SOCl_2$) was employed as a reagent, **8a** was obtained in *ca.* 55%. Although the reaction proceeded rapidly even at room temperature, it produced structurally undefined by-products (~10%) which were hard to separate from **8a** (entry 8).



Scheme 2. Ring contraction rearrangement of **4a** and selected NOE correlations of **8a**

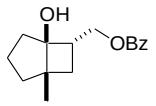
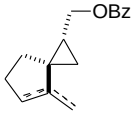
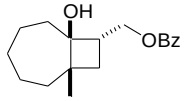
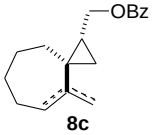
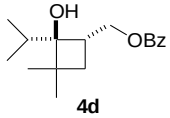
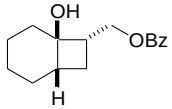
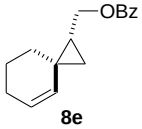
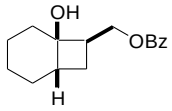
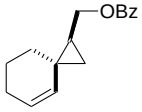
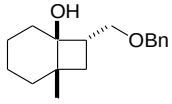
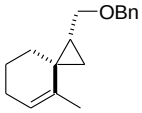
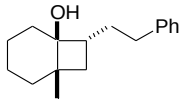
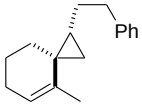
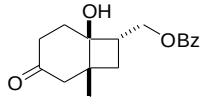
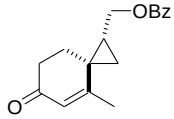
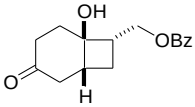
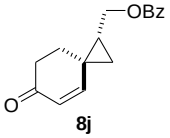
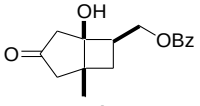
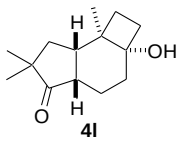
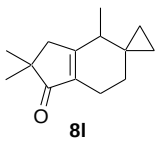
Having established the optimal conditions for the ring contraction reaction, we intended to determine its scope and limitations with respect to the cyclobutanols bearing varied fused rings and substituents (Table 2). Reactions of bicyclo[3.2.0]heptanol **4b** and [5.2.0]nonanol **4c** furnished the corresponding spirocyclopropanes **8b** and **8c**, respectively, in good yields (entries 1 and 2). Differently from the reaction of bicyclo[4.2.0]octanol **4a** giving *endo*-olefin **8a**, **8b** and **8c** were obtained as mixtures of *endo*- and *exo*-olefinic isomers. On the other hand, no rearrangement occurred in the reaction of monocyclic cyclobutanol **4d** (entry 3). It should be mentioned that the rearrangement proceeded in a stereospecific manner. Thus, diastereoisomeric bicyclo[4.2.0]octanols **4e** and **4f** gave the spiro[4.2]octenes **8e** and **8f**, respectively, in moderate yields as a single isomer (entries 4 and

Table 1. Optimization of reaction conditions

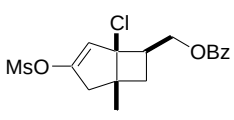
entry	reagents	solvent	temp. (°C)	time (h)[a]	%yield of **8a**
1	Ac_2O (5.0 eq), $Sc(OTf)_3$ (4 mol%)	MeCN	50	6	41
2	MsCl (4.5 eq), 2,6-lutidine (6.0 eq)	MeCN	50	5	42
3	MsCl (4.5 eq), 2,6-lutidine (6.0 eq)	DCE	80	3	31
4	MsCl (4.5 eq), 2,6-lutidine (6.0 eq)	DMF	50	5	41
5	MsCl (4.5 eq)	2,6-lutidine	50	2	70
6	MsCl (2.0 eq)	2,6-lutidine	50	10	65
7	MsCl (4.5 eq)	2,6-lutidine	rt	8	69
8	$SOCl_2$ (2.5 eq), Et_3N (5.0 eq)	DCM	rt	0.25	*ca* 55[b]

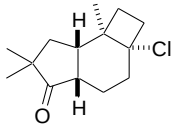
[a] Reaction time was determined when complete consumption of 4a was monitored on TLC. [b] Inseparable byproducts were contained. Ac = acetyl, Tf = trifluoromethanesulfonyl, Ms = methanesulfonyl, DCE = 1,2-dichloroethane, DMF = dimethylformamide

Table 2. Scope of Ring contraction rearrangement[a]

entry	substrates	products	%yield
1	 **4b**	 **8b**	63 (*endo* : *exo* = 3 : 1)[d]
2	 **4c**	 **8c**	62 (*endo* : *exo* = 1 : 10) [d]
3	 **4d**	—	0
4	 **4e**	 **8e**	43
5	 **4f**	 **8f**	42
6	 **4g**	 **8g**	70
7	 **4h**	 **8h**	49
8[b]	 **4i**	 **8i**	82
9	 **4j**	 **8j**	58
10	 **4k**	—	0[e]
11[c]	 **4l**	 **8l**	50[f]

[a] Reactions were carried out using 4 (0.10 mmol) and MsCl (4.5 eq) in 2,6-lutidine (1 M) at 50 °C for 2-20 h, unless otherwise mentioned. [b] at 70 °C. [c] MsCl (4.5 eq), NEt_3 (6.0 eq) in DCM at 0 °C to rt. [d] The ratios (endo : exo) were determined by ^1H NMR. [e] **9k** was obtained as a major product in 58% yield. [f] **10l** was obtained as a by-product in 30% yield.


9k


10l

5). Compounds **4g** and **4h** bearing ether and alkyl side chains, respectively, on the cyclobutane ring also afforded the corresponding spirocyclic compounds in moderate to good yield (entries 6 and 7). The result indicates that the contribution of the oxygen atom to stabilize the cationic intermediate is not crucial. Substrates **4i** and **4j**, which are installed a keto-carbonyl groups on the cyclohexane ring, underwent the rearrangement smoothly to furnish spirocyclic enones **8i** and **8j**, respectively, in high yield (entries 8 and 9). On the contrary, in the reaction of bicyclo[3.2.0]heptanone **4k**, only chloride having enol sulfonate moiety **9k** was obtained in 50% yield. No desired spiro-cyclopropane was observed under the conditions tested (entry 10). To elucidate the effect of a benzoyloxymethyl substituent on the reactivity, the tricyclic substrate **4l** bearing no substituent on the cyclobutane ring was prepared. Its reaction proceeded to give cyclopropane **8l** in 50% yield along with chloride **10l** in 30% yield (entry 11). Formation of **10l** indicates that the reaction would proceed via the generation of a cyclobutyl cation via mesylate of **4l**. It is noteworthy that the reaction of **4l** into **8l** is reasonably consistent with the proposed biosynthetic route of illudins from protoilludanes.[4]

The proposed reaction mechanism of the ring contraction rearrangement was summarized in Figure 3. After the sulfonylation of the tertiary hydroxyl group of **4**, the corresponding carbocationic intermediate **11** can be generated.[15] Then, the adjacent C-C bond to the cation in the cyclobutane ring of **11** can rearrange to give spirocyclic cation **12**. Finally, irreversible deprotonation would result in spiro[n.2]alkene **8**. The preferable production of spiro-cyclopropanes from fused-cyclobutanols can be explained as follows: A release of strain energy of the cyclobutyl cation can act as a driving force for the rearrangement because the sp_2-like geometry of the carbocation on cyclobutane ring (**11**) would be unfavourable compared to that on the medium-sized ring (**12**). In this respect, migration of R^1-R^3 substituents, which also result in the formation of the corresponding cyclobutyl cation intermediates, can

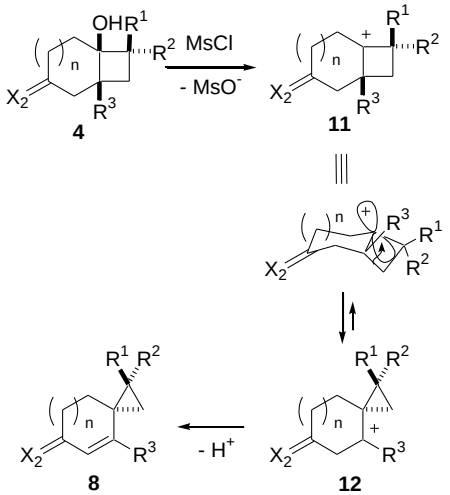


Figure 3. Proposed mechanism for ring contraction rearrangement

be ruled out. Moreover, strain energy of a fused-system itself would be a trigger to rearrange into spiro-system with migration of C-C bond in cyclobutane ring. Clearly, no rearrangement was detected in the reaction of the monocyclic system (entry 3 in Table 2). Beyond our expectations, the desired rearrangement also proceeds in the reaction of **4e**, **4f**, **4j** (R^3 = H), although secondary cation **12** would be generated as an intermediate from tertiary cation **11** (entries 4,5,9 in Table 2). Keto carbonyl group in cyclohexane ring (substrates **4i** and **4j**) would accelerate the final elimination step and, therefore, resulted in higher yielding of **8**.

Next, we considered stereoelectronic effects on the reactivity in order to learn why rearrangement does not occur in the reaction of substrate **4k**. X-ray crystallographic structures of **4i** and **4k** and their Newman projections viewed along the ring juncture are shown in Figure 4.[16] The reaction begins with the generation of the carbocation intermediate **11**. The structure of should be comparable to that of the substrate **4** because a tetrahedral conformation (sp^2 hybridyzed carbon) of the cationic carbon atom at the ring juncture position would be more unstable than a sp^3-like tetrehedral one. Thus, the orientation of the p-orbital of cation **11** would be approximated to that of the hydroxyl σ bond of **4**. It is found that the dihedral angle between the hydroxyl substituent and the migrating C-C bond of **4i** is *ca*. 137°. Namely, the p-orbital and the $\sigma_{C\text{-}O}$ bonding of intermediate **11** would overlap to some degree and, therefore, the rearrangement produces **8i**. In contrast, of the angle for **4k** is almost perpendicular (102°), which would rule out the rearrangement. Suitable crystals for X-ray analysis of the other substrates **4** could not be obtained, but X-ray crystallographic analysis of cyclobutanols **13b** and **13j**, which are synthetic intermediates of **4b** and **4j**, respectively, were performed. The dihedral angle between C-OH bond and C-C bond for **7b** and **13j** are 126° and 143°, respectively (see supporting information). The observation would agree with the results that **4b** and **4j** proceed ring contraction reaction.

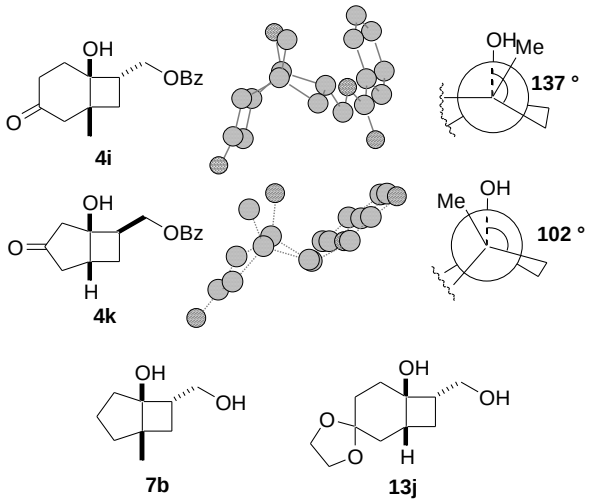


Figure 4. X-ray structures and Newman projections of **4i** and **4k**. Structures of **7b** and **13j**.

Conclusion

In conclusion, an unusual ring contraction rearrangement giving spirocyclic cycropropanes from fused-cyclobutanols is described. It is found that the strain energy of substrates derived from an additional fused-ring and the stereoelectronic effect of the migrating σ-bond are important factors. It is noteworthy that the rearrangement proceeds in a stereospecific manner. Moreover, we demonstrated the biomimetic synthesis of **8l** from **4l**, which corresponds to illudane and the protoilludane skeleton, respectively. Further studies involving the synthesis of illudines and the biological evaluation of synthetic **8** are ongoing in our laboratory.

Experimental Section

General: All reactions were carried out under a positive atmosphere of argon in dried glassware unless otherwise noted. Solvents and materials were obtained from commercial suppliers and used without further purification. Column chromatography was performed on Merck silica gel 60 (230-400 mesh). Reactions and chromatography fractions were analyzed employing pre-coated silica gel plate (Merck Silica Gel 60 F_{254}). All melting points were measured on YANACO MP-500P micro melting point apparatus and are uncorrected. IR spectra were measured on JASCO FT/IR-410. The ^{1}H and ^{13}C NMR spectra were recorded on JEOL AL-400 or JEOL ECP-500 with tetramethylsilane as internal standard. Low-resolution and high-resolution mass spectra were recorded on JEOL JMS-01SG-2 or JMS-HX/HX 110A mass spectrometer. X-ray crystal analyses were performed on Rigaku RAPID-S.

General procedure for ring contraction rearrangement of 4: To a solution of **4** (0.10 mmol) in 2,6-lutidine (0.10 mL) was added MsCl (0.45 mml) at ambient temperature under argon atmosphere. After being stirred at 50 °C, the resulting mixture was quenched with *sat* NH_4Cl. The aqueous layer was extracted with AcOEt three times. The combined organic layers were washed with brine, dried with Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by silica gel chromatography (hexane-AcOEt) to give **8**.

(1*R,3*R**)-1-Benzoyloxymethyl-4-methylspiro[2.5]oct-4-en (8a)**: Colorless oil, ^{1}H NMR (500 MHz, [D_1]chloroform): δ = 8.06 (d, *J* = 7.5 Hz, 2H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.44 (dd, *J* = 7.5, 7.5 Hz, 2H), 5.51 (s, 1H), 4.55 (dd, *J* = 11.5, 6.9 Hz, 1H), 4.27 (dd, *J* = 11.5, 8.0 Hz, 1H), 2.15-2.05 (m, 2H), 1.75-1.69 (m, 2H), 1.64-1.58 (m, 3H), 1.42 (s, 3H), 1.10 (dd, *J* = 8.6, 5.2 Hz, 1H), 0.40 ppm (t, *J* = 5.2 Hz, 1H); ^{13}C NMR (126 MHz, [D_1]chloroform): δ = 166.7, 135.3, 132.8, 130.5, 129.6, 128.3, 123.4, 65.6, 29.5, 25.9, 25.3, 22.4, 20.0, 18.2, 16.3 ppm; IR (neat): ν 2926, 2857, 1719 cm^{-1}; LRMS (FAB): *m/z* 257 (M^+ + 1); Anal. Calcd. for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86; Found: C, 79.72; H, 8.13.

(1*R,3*R**)-1-Benzoyloxymethyl-4-methylspiro[2.4]hept-4-ene (8b: major isomer):** colorless oil; ^{1}H NMR (500 MHz, [D_1]chloroform): δ = 8.06 (dd, *J* = 8.3, 1.7 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.45 (dd, *J* = 8.3, 7.5 Hz, 2H), 5.41 (s, 1H), 4.48 (dd, *J* = 11.7, 7.1 Hz, 1H), 4.17 (dd, *J* = 11.7, 8.0 Hz, 1H), 2.44-2.36 (m, 2H), 2.18-2.11 (m, 1H), 1.96-1.83 (m, 1H), 1.50-1.46 (m, 1H), 1.42 (d, *J* = 1.9 Hz, 3H), 1.00 (dd, *J* = 9.0, 5.1 Hz, 1H), 0.49 ppm (t, *J* = 5.1 Hz, 1H); ^{13}C NMR (126 MHz, [D_1]chloroform): δ = 166.7, 141.2, 132.8, 130.5, 129.6, 128.3, 124.1, 66.8, 35.0, 29.8, 29.0, 17.9, 15.1, 11.5 ppm; IR (neat): ν 2948, 2852, 1718 cm^{-1}; LRMS (FAB): *m/z* 243 (M^+ + 1); Anal. Calcd. for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86, found: C, 79.72; H, 8.13.

(1*R,3*R**)-1-Benzoyloxymethyl-4-methylenespiro[2.6]nonane (8c: major isomer)**: colorless oil; ^{1}H NMR (500 MHz, [D_1]chloroform): δ = 8.07 (d, *J* = 7.6 Hz, 2H), 7.57 (t, *J* = 7.0 Hz, 1H), 7.44 (dd, *J* = 7.6, 7.0 Hz, 2H), 5.51 (s, 1H), 4.71 (s, 1H), 4.65 (s, 1H), 4.57 (dd, *J* = 11.7, 6.3 Hz, 1H), 4.27 (dd, *J* = 11.7, 9.3 Hz, 1H), 2.39-2.28 (m, 2H), 1.80-1.69 (m, 2H), 1.67-1.49 (m, 6H), 1.40-1.36 (m, 1H), 1.05 (dd, *J* = 9.0, 5.1 Hz, 1H), 0.51 ppm (t, *J* = 5.1 Hz, 1H); ^{13}C NMR (126 MHz, [D_1]chloroform): δ = 166.7, 155.7, 132.8, 130.4, 129.6, 128.3, 109.1, 65.9, 35.9, 33.3, 29.9, 29.0, 28.9, 27.4, 25.3, 19.7 ppm; IR (neat): ν 2925, 2853, 1719 cm^{-1}; LRMS (FAB): *m/z* 271 (M^+ + 1); Anal. Calcd. for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20, found: C, 80.15; H, 8.44.

(1*R,3*S**)-1-Benzoyloxymethylspiro[2.5]oct-4-ene (8e):** Colorless oil; ^{1}H NMR (500 MHz, [D_1]chloroform): δ = 8.06 (d, *J* = 8.6 Hz, 2H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.44 (dd, *J* = 8.6, 7.3 Hz, 2H), 5.68 (td, *J* = 10.0, 3.6 Hz, 1H), 5.00 (td, *J* = 10.0, 2.0 Hz, 1H), 4.55 (dd, *J* = 11.7, 6.6 Hz, 1H), 4.27 (dd, *J* = 11.7, 8.8 Hz, 1H), 2.09-2.04 (m, 2H), 1.80-1.69 (m, 3H), 1.65-1.51 (m, 1H), 1.33-1.25 (m, 1H), 0.83 (dd, *J* = 8.8, 4.9 Hz, 1H), 0.40 ppm (t, *J* = 4.9 Hz, 1H); ^{13}C NMR (126 MHz, [D_1]chloroform): δ = 166.7, 134.7, 132.8, 130.5, 129.6, 128.3, 126.2, 65.5, 28.0, 25.1, 23.8, 22.9, 22.2, 19.2 ppm; IR (neat): ν 2928, 1718 cm^{-1}; LRMS (FAB) *m/z* 242 (M^+); HRMS (FAB) calcd for $C_{16}H_{18}O_2$ (M^+): 242.1307, found: 242.1306.

(1*R,3*R**)-1-Benzoyloxymethylspiro[2.5]oct-4-ene (8f):** colorless oil ; ^{1}H NMR (500 MHz, [D_1]chloroform): δ = 8.05 (d, *J* = 7.1 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.44 (dd, *J* = 7.3, 7.1 Hz, 2H), 5.78 (td, *J* = 10.0, 3.7 Hz, 1H), 5.32 (td, *J* = 10.0, 2.2 Hz, 1H), 4.46 (dd, *J* = 11.7, 7.1 Hz, 1H), 4.20 (dd, *J* = 11.7, 8.3 Hz, 1H), 2.10-2.06 (m, 2H), 1.81-1.69 (m, 2H), 1.65 (dd, *J* = 9.5, 3.6 Hz, 1H), 1.38-1.32 (m, 1H), 1.29-1.22 (m, 1H), 0.90 (dd, *J* = 8.5, 5.1 Hz, 1H), 0.65 ppm (t, *J* = 5.1 Hz, 1H); ^{13}C NMR (126 MHz,

[D_1]chloroform): δ = 166.7, 132.7, 130.6, 129.6, 129.6, 128.5, 128.3, 66.1, 34.5, 25.6, 25.3, 23.1, 22.3, 19.9 ppm; IR (neat): ν 2925, 1714 cm^{-1}; LRMS (FAB) *m/z* 242 (M^+); HRMS (FAB) calcd for $C_{16}H_{18}O_2$ (M^+): 242.1307, found: 242.1303.

(1*R,3*R**)-1-Benzyloxymethylspiro[2.5]oct-4-ene (8g):** colorless oil ; ^{1}H NMR (500 MHz, [D_1]chloroform): δ = 7.35-7.32 (m, *4*H), 7.28-7.26 (m, 1H), 5.49 (s, 1H), 4.56 (d, *J* = 12.0, 1H), 4.50 (d, *J* = 12.0, 1H), 3.54 (dd, *J* = 10.3, 7.4 Hz, 1H), 2.09-2.02 (m, 2H), 1.77-1.61 (m, 3H), 1.51-1.42 (m, 2H), 1.40 (s, 3H), 1.02 (dd, *J* = 9.2, 4.6 Hz, 1H), 0.25 ppm (t, *J* = 4.6 Hz, 1H); ^{13}C NMR (126 MHz, [D_1]chloroform): δ = 138.6, 135.8, 128.3, 127.7, 127.5, 123.1, 72.7, 70.3, 29.5, 25.9, 24.8, 22.5, 21.0, 18.2, 16.3 ppm; IR (neat): ν 2926, 2855 cm^{-1}; LRMS (FAB) *m/z* 243 (M^+ + 1); Anal. Calcd. for $C_{17}H_{22}O$: C, 84.25; H, 9.15, found: C, 84.20; H, 9.25.

(1*R,3*R**)-4-Methyl-1-[(2-phenyl)ethyl]spiro[2.5]oct-4-ene (8h):** colorless oil ; ^{1}H NMR (500 MHz, [D_1]chloroform): δ = 7.29-7.25 (m, 2H), 7.20-7.16 (m, 3H), 5.47 (s, 1H), 2.71 (t, *J* = 8.0, 1H), 2.09-2.02 (m, 2H), 1.84-1.76 (m, 1H), 1.70-1.54 (m, 4H), 1.49-1.44 (m, 1H), 1.37 (s, 3H), 1.12-1.05 (m, 1H), 0.93 (dd, *J* = 9.2, 4.6 Hz, 1H), 0.05 ppm (t, *J* = 4.6 Hz, 1H); ^{13}C NMR (126 MHz, [D_1]chloroform): δ = 142.6, 136.8, 128.4, 128.2, 125.6, 122.2, 36.4, 31.0, 29.6, 26.0, 24.7, 22.7, 21.6, 18.4, 18.0 ppm; IR (neat): ν 2922, 2855 cm^{-1}; LRMS (FAB) *m/z* 226 (M^+); Anal. Calcd. for $C_{17}H_{22}$: C, 90.20; H, 9.80, found: C, 90.25; H, 9.71.

(1*R,3*R**)-1-Benzoyloxymethyl-4-methyl-spiro[2.5]oct-4-en-6-one (8i):** white solids; M.p. 57-58 °C (Hexane/EtOAc); ^{1}H NMR (400 MHz, [D_1]chloroform): δ = 8.02 (dd, *J* = 8.5, 1.4 Hz, 2H), 7.58 (tt, *J* = 7.5, 1.4 Hz, 1H), 7.45 (dd, *J* = 8.5, 7.5 Hz, 2H), 5.97 (s, 1H), 4.75 (dd, *J* = 12.0, 6.1 Hz, 1H), 4.21 (dd, *J* = 12.0, 9.3 Hz, 1H), 2.58-2.43 (m, 2H), 2.12-1.98 (m, 2H), 1.88-1.80 (m, 1H), 1.70 (d, *J* = 1.2 Hz, 3H), 1.35 (dd, *J* = 9.3, 5.4 Hz, 1H), 0.81 (t, *J* = 5.4 Hz, 1H) ppm; ^{13}C NMR (126 MHz, [D_1]chloroform): δ = 199.1, 166.4, 163.5, 133.2, 129.9, 129.5, 128.5, 127.7, 64.5, 36.8, 28.1, 26.3, 22.5, 19.3, 17.1 ppm; IR (neat): ν 2955, 1717, 1665 cm^{-1}; LRMS (FAB) *m/z* 271 (M^+ + 1); HRMS (FAB) calcd for $C_{17}H_{19}O_3$ (M^+ + 1): 271.1334, found: 271.1331.

(1*R,3*S**)-1-Benzoyloxymethylspiro[2.5]oct-4-en-6-one (8j):** white solids; M.p. 65-66 °C (Hexane/EtOAc); ^{1}H NMR (400 MHz, [D_1]chloroform): δ = 8.03 (d, *J* = 7.1 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.45 (dd, *J* = 7.4, 7.1 Hz, 2H), 6.23 (d, *J* = 10.0 Hz, 1H), 5.99 (d, *J* = 10.0 Hz, 1H), 4.73 (dd, *J* = 12.0, 5.8 Hz, 1H), 4.14 (dd, *J* = 12.0, 9.3 Hz, 1H), 2.54 (td, *J* = 7.8, 1.7 Hz, 1H), 2.17-2.10 (m, 1H), 2.06-1.99 (m, 1H), 1.73-1.66 (m, 1H), 1.18 (dd, *J* = 9.0, 5.4 Hz, 1H), 0.95 (t, *J* = 5.4 Hz, 1H) ppm; ^{13}C NMR (126 MHz, [D_1]chloroform): δ = 199.2, 166.4, 157.3, 133.2, 129.9, 128.5, 128.1, 64.4, 36.6, 26.4, 25.0, 23.9, 19.2 ppm; IR (neat): ν 2957, 1717, 1672 cm^{-1}; LRMS (FAB) *m/z* 257 (M^+ + 1); HRMS (FAB) calcd for $C_{16}H_{17}O_3$ (M^+ + 1): 257.1178, found: 257.1182.

3,3,9-Trimethylbicyclo[4.3.0]nonan-1(5)en-4-one-8-spirocyclopropane (8l): colorless oil; ^{1}H NMR (400 MHz, [D_1]chloroform): δ = 2.49 (dt, *J* = 18.3, 3.1 Hz, 1H), 2.30-2.05 (m, 3H), 1.93-1.82 (m, 1H), 1.68 (td, *J* = 7.6, 7.1 Hz, 1H), 1.12 (s, 3H) , 1.12 (s, 3H) , 1.11 (s, 3H), 0.96 (ddd, *J* = 13.5, 5.8, 2.9 Hz, 1H) ppm; ^{13}C NMR (126 MHz, [D_1]chloroform): δ = 203.3, 174.1, 135.4, 45.4, 43.5, 40.8, 27.6, 25.3, 25.3, 21.3, 20.0, 16.5, 12.8, 9.8 ppm; IR (neat): ν 2928,1699,1645 cm^{-1}; LRMS (FAB) *m/z* 204 (M^+); HRMS (FAB) calcd for $C_{14}H_{20}O$ (M^+): 204.1514, found: 204.1497.

Crystal data for 4i.: colorless needles (recryst. from hexane-AcOEt), $C_{17}H_{20}O_4$, monoclinic, space group $P2_1/n$, *a* = 11.7971(6) Å, *b* = 7.5796(3) Å, *c* = 17.7477(8) Å, β = 104.283(3)°, *V*= 1537.90(12) $Å^3$, *Z* = 4, D_{calc} = 1.245 g/cm^3, *R* = 0.0477, R_w = 0.074, GOF = 0.854.

Crystal data for 4k: colorless platelets (recryst. from hexane-AcOEt), $C_{16}H_{18}O_4$, triclinic, space group *P*-1, *a* = 6.7625(6) Å, *b* = 9.4963(7) Å, *c* = 11.2202(9) Å, β = 101.648(2)°, β = 96.981(3)°, β = 100.873(3)°, *V*= 683.40(1) $Å^3$, *Z* = 2, D_{calc} = 1.333 g/cm^3, *R* = 0.0780, R_w = 0.1730, GOF = 1.108.

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[15] As an alternative possible mechanism, a concerted S_N2-type rearrangement pathway can be proposed. Thus, both elimination of mesyl group and migration of C-C bond would occur concertedly giving spiro-cyclopropanes. Formation of chloride **10l** would suggest formation of cationic intermediate **11**. Thus, a stepwise mechanism would be preferable. .Further study to throw light to the reaction mechanism is ongoing.

[16] CCDC 758893 (**4i**), 758894 (**4k**) 758895 (**7b**) and 758896 (**13k**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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Ring Contraction

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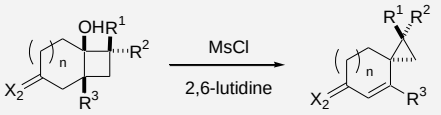
Stereocontrolled Synthesis of Spiro[n.2]alkenes by Ring Contraction of Fused-Cyclobutanols



Rearrangement into cyclopropane from cyclobutane: Unusual ring contraction rearrangement giving spiro-cyclopropanes from fused-cyclobutanols have been developed. It is found that the strain energy of substrates derived from an additional fused-ring and the stereoelectronic effect of the migrating σ-bond are important factors. It is noteworthy that the rearrangement proceeds in a stereospecific manner.